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TOXICOLOGICAL RESEARCH ON CENTRAL NERVOUS SYSTEM EFFECTS OF BORANE FUELS

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NORTH AMERICAN AVIATION, INC.

SEPTEMBER 1961

CONTRACT No. AF 33(616)-7186

BIOMEDICAL LABORATORY
AEROSPACE MEDICAL LABORATORY
AERONAUTICAL SYSTEMS DIVISION
AIR FORCE SYSTEMS COMMAND
UNITED STATES AIR FORCE
WRIGHT-PATTERSON AIR FORCE BASE, OHIO

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CONTRACT No. AF 33(616)-7186
PROJECT No. 7165
TASK No. 71836

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FOREWORD

This is the final report on the program conducted under the provisions of Contract AF 33(616)-7186, Project No. 7165, "Health Hazards of Material and Radiation, "Task No. 71836, "Evaluation and Control of Toxic Chemical Materials," with the Biomedical Laboratory, Aerospace Medical Laboratory, Aeronautical Systems Division.

Anton Tamas, M.D., Toxic Hazards Section, Physiology Branch Biomedical Laboratory, served as project officer.

Toby Freedman, M.D., Corporate Flight Surgeon, directed the project. Electrographic Laboratories, under the direction of Mr. William Shuler, made the EEG tracings and obtained exposure histories. Richard Walter, M.D., and Kenneth Blinn, M.D., served as EEG interpreters. Charles Schoettlin, M.D., and George Cianko contributed to the compilation of the final report.

ABSTRACT

This report describes the research conducted by North American Aviation, Inc., Los Angeles, California, on the central nervous system subsequent to accidental human exposure to boron hydrides. Serial electroencephalographic (EEG) tracings were used to identify the effects. Results of the study indicate little or no central nervous system damage was experienced by the participants. Methods, machines, and techniques used are described in detail. A complete data summary of all subjects tested is included.

PUBLICATION REVIEW

Jos. M. Quashnock

JOS. M. QUASHNOCK
Colonel, USAF, MC
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INTRODUCTION

The four seemingly unrelated items described below each contributed to the inauguration of this project.

On 5 November 1958 the Engineering Research Unit was conducting routine pentaborane firings at North American Aviation, Inc., Propulsion Field Laboratory, Santa Susana, California. One research engineer working in the area, patient #306352, wore no protective mask or equipment. At 3:30 PM he felt nervous. After this he had a lapse of memory. After arriving at work on the following morning, it was noted that he was sweating profusely and was very confused. He spoke slowly because of an inability to think, and was unable to describe what was wrong. He had a wide-awake stare and a recent memory loss. Upon questioning, he complained of aching in all of his muscles. It was observed that when he was touched he developed muscle tremors. He complained of having not slept the previous night. He noted,on attempting to walk,that his "knees felt stiff, and back and hips felt as though they were slipping backwards. It was a funny feeling." Oxygen therapy was started. At one time during observation he developed tetany and opisthotonos.

The Flight Surgeon at North American Aviation, Inc., Los Angeles, California, was conducting a series of electroencephalograms on pilots to determine central nervous system damage from in-flight injuries. Obvious abnormalties were observed on the tracings made on the pilots.

At the East Parking Lot Fuel Laboratory of North American Aviation, Inc., a group of chemists were investigating the properties of high-energy fuels. Within two months of commencing this research, minute amounts of the fuel had been spilled onto the chemist's hands and vapor had been inhaled. The people so exposed developed frequent headaches in the frontal and occipital regions. These headaches persisted for 1 to 2 hours.

Literature available at the time* stated that symptoms of light headedness, dizziness, headaches, tremors, and muscle spasms had occurred in persons exposed to boron hydride fuels. Animal toxicity studies on pentaborane and decaborane revealed hyperactivity of the central nervous system. EEG's performed on animals suggested the central nervous system disturbances which occurred were possibly cortical in origin rather than from hypoxia due to pulmonary edema.

These bits of information were utilized in developing the protocol on which this project was based. It was anticipated that the boron hydride fuels would be handled in increasing quantities during the next few years. In addition, it was felt that some means of medical surveillance must be developed which would give an index of the degree of central nervous system damage which an employee has sustained. The industrial physician must decide

1. When can the man who has recovered clinically go back to his job handling these fuels?
2. Did any permanent damage occur?
3. Did the first exposure so sensitize the patient that any subsequent exposure would precipitate symptoms?

There was need for a laboratory tool which would tell the physician when physiologic recovery was complete. The EEG appeared to be a simple laboratory tool for predicting the extent, type, and reversibility of central nervous system damage from boron hydride exposure.

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*Tamas, Anton A.: State of the Art Report on Health Hazards of Borane Fuels and Their Control, Aerospace Medical Laboratory, ASD, Wright-Patterson Air Force Base, Ohio

PROGRAM APPROACH

STUDY GROUP

The intent of this study was to take serial EEG's on a group of people who are likely to be exposed to boron hydrides. Because too few people at North American Aviation, Inc., were handling these materials to provide adequate data for clinical evaluation, a similar group was sought. These men working on the pentaborane projects at Edwards Rocket Base (a facility of Edwards Air Force Base) were a logical choice. Both groups had similar potential for borane exposure. The men were of similar age, race, and occupation, yet were far different from those people on whom EEG's were usually taken. Most people having EEG's have had prior symptoms and would be more apt to show EEG changes than the men under study. On the other hand the rocket propellant handlers would be more likely to show abnormalities than a group of normal persons because it was discovered that the athletic rocket propellant handlers were more likely to have suffered from head trauma as a result of sports during school years. To learn what baseline to expect in the potentially exposed groups, it was thought appropriate to include men of the same physical makeup, but who had different occupations. Thirty-six men at Edwards Rocket Base who had no history of contact with boron hydrides were selected as controls.

Through difficulty in implementing the experimental design, the men selected as controls were not of the same age as the propellent handlers. The selection of the control group of men who were in their early twenties created a problem in the correlation of interpreted records. The human brain does not mature electroencephalographically until the age of 23 or 24 years. Under resting conditions, the EEG of a subject 21 years old may show sporadic, scattered, slow waves; but, during hyperventilation, even a 24-year old subject may develop slow wave activity.

EEG SCHEDULE

The plan of the study was to take serial EEG's at 3-month intervals on each man participating. This was was not realized. A group of firemen at North American Aviation, Inc., Los Angeles Division were dropped from the study after their first EEG because they refused to submit to a second EEG. This loss had no affect on the final tabulation because their initial EEG had been taken prior to the contract. A loss that was acutely felt, however, was the transfer of 14 members of the control group to another Air Force base. The final tally showed that only 9 persons had all 4 EEG's; 33 persons had 3 tracings; each of the remaining 99 had only 2 tracings. Only those persons who had at least two EEG's were included in the final tabulation.

Total of 153

MACHINES AND TECHNICIANS

Two models of Offner 8-channel machines were used in this study. Since the electroencephalographer prefers records made on a permanent type machine, an Offner Model D was used whenever space was available. A portable Offner Model T was used when space was at a premium. The two machines produce technically comparable tracings. The advantage of the Model D is its lack of sensitivity to changes in temperature and humidity. Only six tracings in the entire study had to be repeated because of machine defect. The EEG interpreter felt that all other tracings taken during the study were of adequate quality.

Four technicians, all members of the Western Society of EEG Technicians, operated the machines and observed the subjects for eyelid and muscle movement, and for drowsiness.

EXAMINATION PROCEDURE

The subject, who reported to the first-aid station according to schedule, was simply told that he was to have an EEG. To ensure a high blood sugar level, the subject was required to drink 100 grams of glucose in whisky sour mix. The flavoring mixture was added during the latter phases of the study to improve palatability because of complaints of tase and occasional nausea. The simple sugar mix was taken approximately 30 minutes before the tracing was started.

The subject was told only enough about the study to gain his cooperation. Details of the study were not elaborated, although specific questions were answered to the best of the technician's ability.

The patient was placed in the examining room on a bed, and made as comfortable as possible. He was instructed to relax and to keep his eyes closed except when he was asked to open his eyes occasionally to avoid drowsiness.

THE EEG RECORD

ORIGIN OF ELECTRICAL ACTIVITY

It is fairly certain that the electrical signals recorded from the scalp originate in the outer layer of the brain, the cortex. This layer contains a great many nerve cell bodies and their processes. Many of the details of the physiology of the neurons in the cortex are unknown, including some aspects of the origin of their electrical activity. However, in the last few years, it has become apparent that the brain waves, as recorded from the scalp, originate from currents of a longer lasting type than those appearing in the more familiar peripheral nerve. These long-lasting or steady potentials exist primarily between the apical dendrite and the cell body itself. There probably is a summation of these individual, extremely minute currents because the majority of the apical dendrites are aligned in a parallel fashion.

These electrical signals oscillate at anywhere between 1 and 30 times per second. It is supposed that an area called a "pacemaker," analogous to the structure within the heart is in operation in some portion of the brain. Currently a good deal of experimental evidence indicates that the pacemaker may be located in the thalamus and brainstem. These areas presumably "control" the steady potentials existing at the cortex through connections with cortical neurons. Through this control, the rhythmical fluctuations which are characteristic of the EEG are produced. There is some evidence, however, that the cortex itself may be capable of producing rhythmical activity when its connections are severed from other parts of the brain.

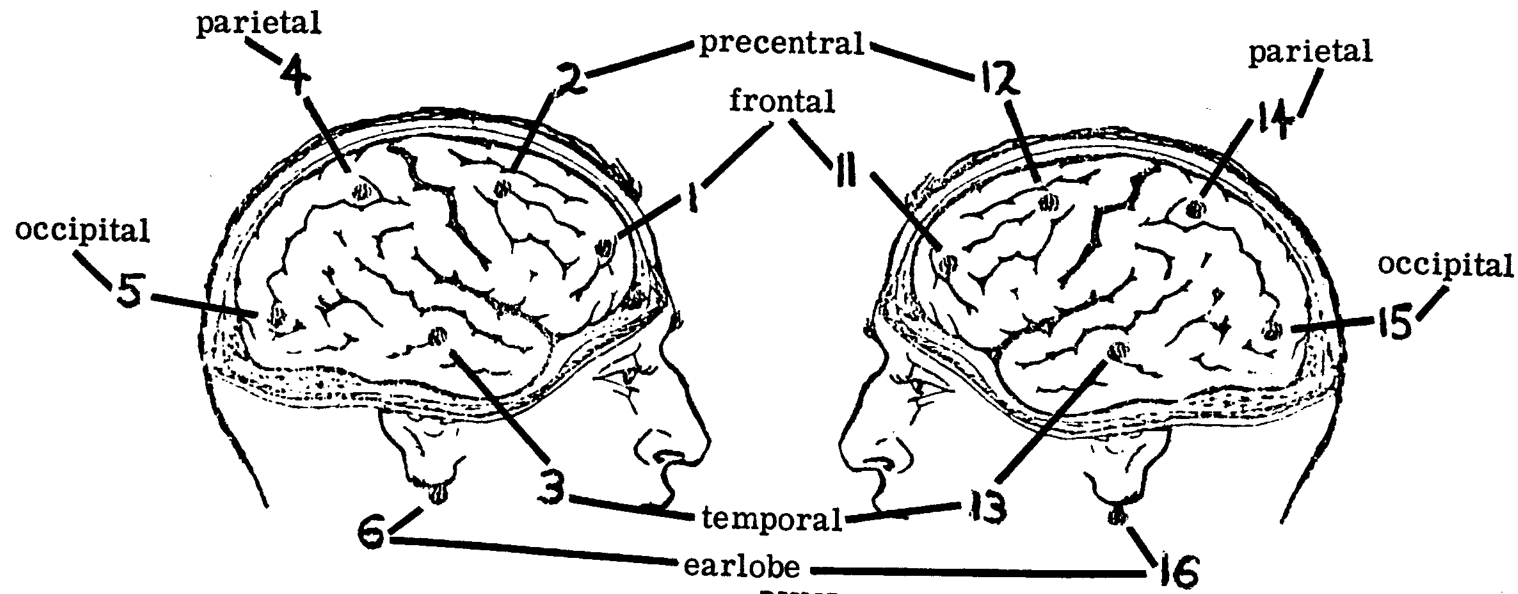
ELECTRODES

Detection of the electrical signals from the brain was accomplished by electrodes consisting of very fine stainless steel needles which were inserted into the scalp. This insertion upon occasion was momentarily painful, but the patient was usually soon unaware of the electrodes' presence.

Many electrical abnormalities originate from a relatively small area so that their detection is only possible when an adequate number of electrodes are strategically placed about the scalp (Fig. 1). All the major areas were covered: the frontal (1, 11), precentral (2, 12), temporal (3, 13), parietal (4, 14), and occipital (5, 15) regions. Electrodes were also placed on the lobe of each ear (6, 16) and on the vertex (subject ground).

THE EEG MACHINE

Thin wires attached the electrodes to the EEG machine. The minute electrical signals, ranging from 5 to 300 millivolts were amplified by a series of tubes or transistors. The information was then transcribed on a moving paper by 8 pens. As only 8 pens were available and 12 electrodes were on the scalp, the technician had to switch the activity from the electrodes periodically so that all areas were recorded. The runs used in this study are listed in Fig.1.



RUNS

1	2	3	4	5	6
1-5	1-2	1-3	1-4	1-5	1-6
1-5	2-3	3-13	4-14	5-15	6-16
1-5	3-4	13-11	14-11	15-11	16-11
1-5	4-5	11-1	11-1	11-1	11-1
1-5	11-12	5-2	5-3	4-2	4-3
1-5	12-13	2-12	3-13	2-12	3-13
1-5	13-14	12-15	13-15	12-14	13-14
1-5	14-15	15-5	15-5	14-4	14-4

RETURN TO RUN 2 FOR HYPERVENTILATION

Figure 1. Electrode Placement

Just as some electrical abnormalities are localized to a small area, some appear only sporadically in time. The duration of the recording had to be long enough to be reasonably certain of recording these sporadic, or transient events. Recordings were continued for about 20 minutes.

As might be appreciated from the small size of the signals to be detected, electrical interference (artifacts) from sources other than the brain constituted a problem. Blinking the eyes, swallowing, coughing, muscular movement, and machine malfunction all induce signals in the record that may obscure or alter the pattern of the brain waves. Though the electroencephalographer could usually identify the origin of these extraneous signals by their wave pattern and general appearance, the technician played a vital role in their elimination. The cause of artifacts was noted directly on the record by the technician; he also noted any other clinical observation that seemed pertinent. In addition, it was the role of the technician to ensure that all of the 8 channels were amplifying the signals from the brain to the same degree. The interpreter requested at least two pages of artifact-free tracing for each run. This meant taking a tracing of 60 to 100 seconds long for each run.

Prior to each recording, the machine was calibrated at 50 microvolts; equalization of all 8 channels was made when necessary. In addition, a standardization from the patient was recorded (Fig. 1, run 1).

EEG INTERPRETATION

LIMITATIONS

The primary cortical origin of the EEG leads to some practical considerations in its use in the detection of cerebral pathology. It may not be possible to elicit any alteration of an abnormal type in the EEG if the diseased area is in the deeper parts of the brain. Such diseased areas, however, may have an effect on the cortical electrical activity by alterations in the connections between the deep areas and the cortex.

Another practical difficulty is that the entire area of the cortex cannot adequately be surveyed from the scalp. A good deal of the cortex lies in folds in the brain substance, the gyri and sulci; and the cortex at the base of the brain in particular is not accessible from the scalp. This situation probably explains, in part, the recording of fairly normal electrical patterns, even though there is known to be some structural change at the base of the brain.

NORMAL PHYSIOLOGY AND THE EEG

The recordings obtained from the brain are in one sense extremely variable from moment to moment--responding to, and influenced by, a host of mechanisms both known and unknown. In another sense, however, the patterns are more constant and predictable; one individual's patterns demonstrate the same general characteristics over long periods of time in spite of the above-mentioned short-term variations. The spread of frequencies obtained in the tracings from man range from

1/2 to 40 or 50 cycles per second (cps). Adults generally show a very rhythmical type of activity between 8 and 13 cps, which appears most prominently over the occipital areas. This is the familiar "alpha" activity.

Among the many variables influencing the brain waves, several stand out as major considerations in the clinical interpretation of the record. The age of the individual influences the type of electrical patterns obtained. A rough continuum is present with newborn infants demonstrating a slower pattern consisting of 1/2 to 3 cps, and adults with 8 to 13 cps activity. Age, then, must be considered in the evaluation of any record regarding normal or abnormal, and a single "normal" standard cannot be used in clinical practice. This alteration of frequencies by age is probably a function of the increase in the complexity and branching of the dendrites in the cortex and not the result of an increase in the number of cells in the brain.

To assign a single "basic" frequency to any but the most exceptional record is a great simplification. At any age there is generally a consistent difference between areas of the head, and these differences must also be evaluated in the interpretation of the record. In adults, the occipital regions characteristically show the most rhythmical, higher amplitude, 8 to 13 cps rhythm.

Dramatic alterations in electrical patterns are induced by varying levels of sleep and drowsiness. The rhythmical 8 to 13 cps activity is obtained most characteristically where the patient is awake, reasonably alert, and has his eyes closed. During drowsiness, slower, 5 to 7 cps waves appear which persist into the stage of light sleep. Added to these frequencies, however, are peculiar "spindles" of 14 cps activity which are prominent over the frontal and central regions during light sleep. During deeper sleep, the tracing consists of higher potential, slower, 1 to 3 cps waves. At the other extreme of alertness, represented by an increased attention or vigilance, the record shows a loss of the familiar 8 to 13 cps activity, and this may be replaced by lower voltage, faster, 15 to 20 cps waves. These electrical changes during sleep are quite constant and reproducible and may serve as an accurate indication of the patient's level of consciousness.

In addition to age and the levels of sleep, the general metabolic state of the individual influences the type of electrical activity obtained. Some of the more important factors in this regard are the state of oxygenation of the blood, the level of circulating carbon dioxide, the blood sugar level, and, to a lesser degree, the patient's metabolic rate. Many of the initial tracings taken on subjects in this study showed minor abnormalities which are compatible with low blood sugar levels. To rule out hypoglycemia, 100 grams of the simple sugar mix was given to each subject. This procedure was used consistently throughout the remainder of the program. In all cases, a repeat tracing was made on persons having an initial EEG interpreted as abnormal with hypoglycemia as the possible etiology. Drugs of many different types also influence the electrical pattern. The barbiturates and benzedrine-like compounds both generally produce a good deal of low voltage, fast 15 to 30 cps activity. To rule out a possible effect of drugs, the technician asked each subject if any medication had been taken during the last 24 hours.

From these considerations it is apparent that the EEG is not like a fingerprint; that it is not dependent upon anatomy alone, but is influenced by a great number of physiological processes (Fig. 2).

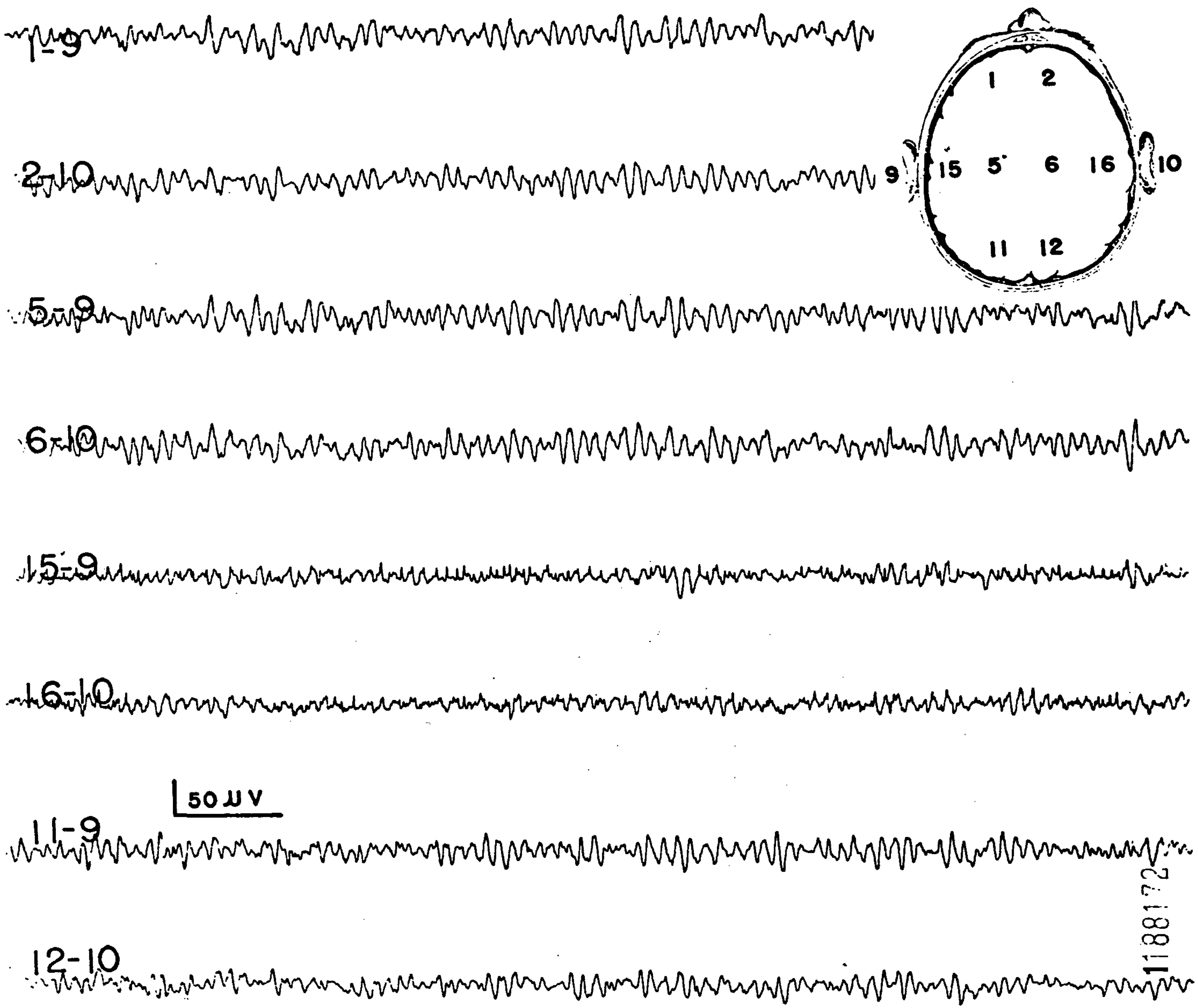


Figure 2. Normal EEG, Adult (NHVO)

It is the electroencephalographer's task to identify correctly the EEG alterations induced by the normal physiological events before consideration can be given to possible electrical abnormalities in the tracing.

ABNORMAL EEG

The types of electrical abnormalities in the resting tracing have been traditionally described as falling into four rather broad groups. The EEG is abnormal because

1. It contains too much "slow" activity (S) (Fig. 3)
2. too much "fast" activity (F), or
3. there are transient or "paroxysmal" abnormalities in the record (P), or
4. because of an electrical event over a single part of the brain, a "focal" abnormality (L), (Fig. 4).

"Abnormally slow" implies that the frequencies obtained are much slower than those usually seen for the patient's chronological age, and that the slowing is not part of the slower activity seen normally in drowsiness or sleep. And what does "abnormally slow" mean that the patient has? Like many other laboratory results, these are nonspecific findings. The slow record reflects an alteration in brain physiology, but a host of pathological processes can reproduce the same electrical picture. A 3 cps wave looks the same regardless of the mechanisms responsible for its production. This is not to say, however, that there are not additional clues in a recording besides the slow activity. Other considerations must be given to the presence or absence of focal abnormalities, the character of the background rhythm, and changes observed in

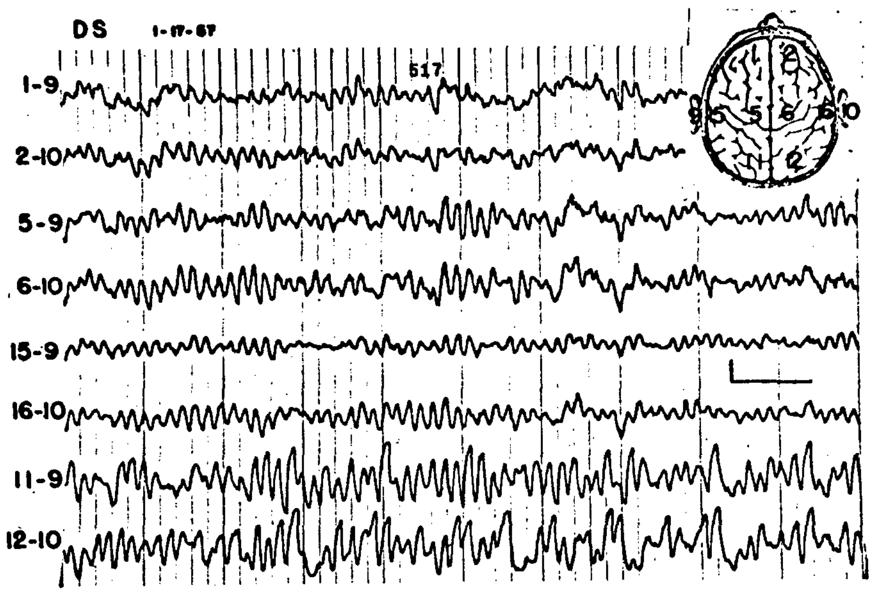


Figure 3. Slow Abnormality (SHVT)

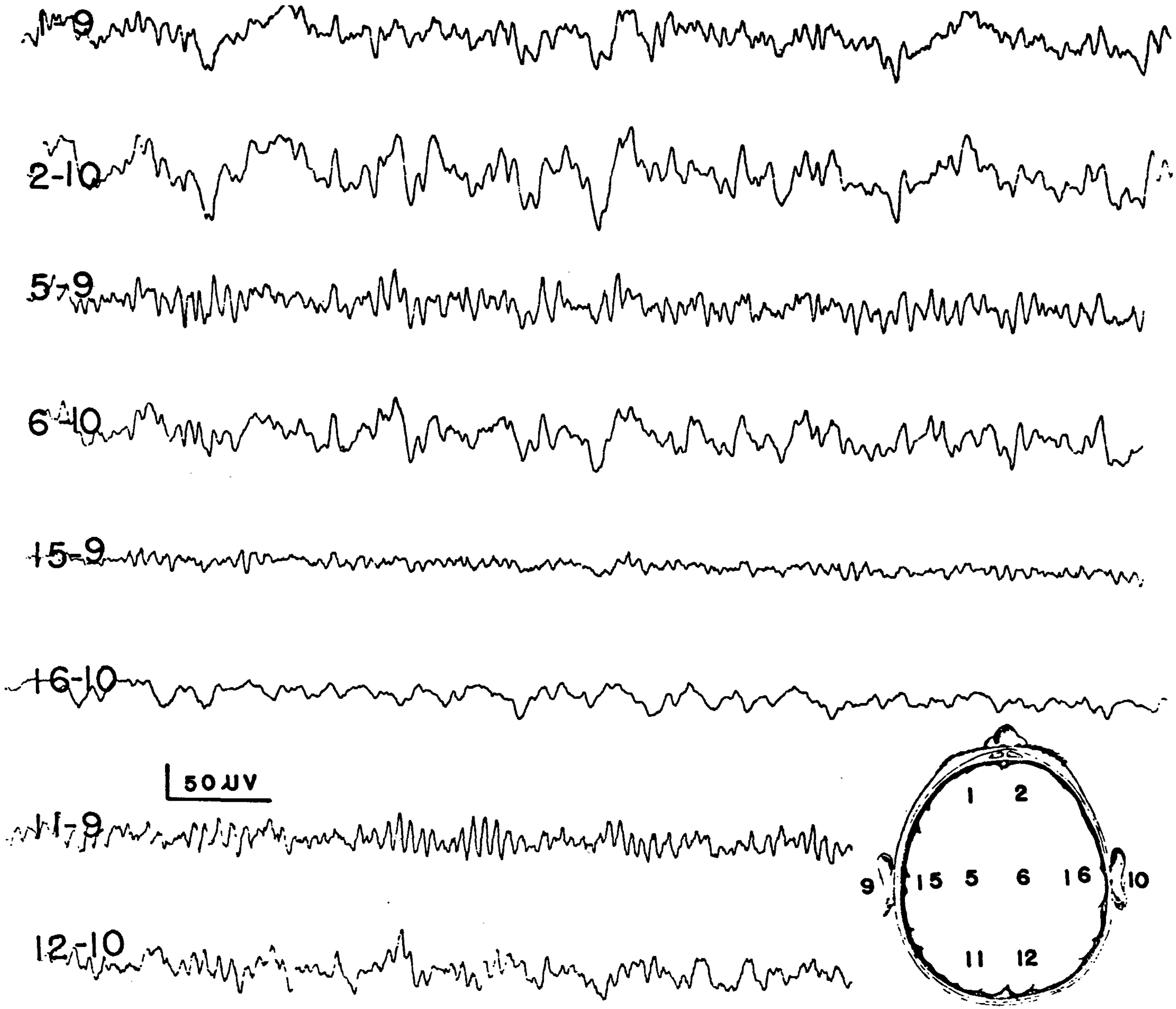


Figure 4. Focal Abnormality, Right Hemisphere (LHVO)

serial recordings. These factors may aid the electroencephalographer in assigning the abnormally slow activity observed to a particular cause.

"Abnormally fast" usually is even less specific regarding cause than is the slow activity. However, it is generally a more benign abnormality, and in many cases the clinical correlations that can be made with an unusual amount of fast EEG activity are quite poor. The most common cause of an unusual amount of fast activity in the EEG is probably related to recent drug ingestion or administration.

A "paroxysmal abnormality" implies that the electrical changes appear in a transient or intermittent fashion. The electrical paroxysms may consist of intermittent slow activity, or they may consist of sudden changes in the amplitude of the waves. Spikes and sharp waves are brief duration signals, often high in amplitude, that always are a rather important indication of central nervous system abnormality. These are often seen in the convulsive disorders and appear as paroxysmal patterns.

"Focal abnormalities" indicate that an area of the brain is not producing normal electrical activity. The abnormality may be an area of slow waves, or fast frequencies, or a region of increased or decreased amplitude, or the site of transient, paroxysmal type of abnormalities. Detection of a focal abnormality may be an important diagnostic clue and is an important consideration in the evaluation of any recording.

HYPERVENTILATION

The caliber of the cerebral blood vessels are known to be considerably influenced by the level of carbon dioxide in the blood. An increased amount of carbon dioxide results in vasodilatation and a decreased amount in vasoconstriction. This mechanism was utilized during the EEG examination by having the subject hyperventilate for a period of time standardized at 3 minutes. Overbreathing for this period reduces the blood carbon dioxide and results in some vasoconstriction with probably mild hypoxic changes in the cerebrum. The subject's electroencethalographic responses may range along a scale from no EEG change during this period (HVO), to the appearance of some slow, 4 to 7 cycles per second "theta" activity (HVT), or to the presence of presistent high potential slow, 1 to 3 cycles per second "delta" activity (HVD). An abnormal response was evaluated in terms of a subject's age, the degree of slowing in the record during this period, and its persistence following hyperventilation. In general, subjects with convulsive disorders and other disturbances of the central nervous system will show a greater electroencephalographic response to hyperventilation than the normals.

The EEG changes resulting from hyperventilation are also influenced in part by the level of the blood glucose. Hypoglycemia could result in a greater amount of slowing or other electrical abnormalities during hyperventilation. It is probable that high blood sugar levels in the physiological range do not suppress electrical abnormalities induced by hyperventilation.

OBTAINING EXPOSURE HISTORIES

A series of EEG's taken on a man working with boron hydrides is useless unless an exposure history is also available. The exposure history ideally contains exact time, date, extent, mode, and severity of exposure. Medical history, physical examination, and progress notes are a desirable adjunct to the EEG. Unfortunately, this research study was not designed to include this information on a systematic basis. It was hoped that the attending physician would compile all the desirable information and make it available for use with the EEG tracings. During the first 2 months of the study, however, the need for adequate systematic exposure histories became very obvious. The task of obtaining this information was delegated to the EEG technician.

A set of standard history questions was asked each man as soon as his tracing had been completed. To avoid loss of the information, answers were recorded directly on the tracing. Age of the worker and whether he was right or left handed was requested by the electroencephalographer as an aid to interpretation. Past history of head trauma and unconsciousness was elicited to gain insight into observed tracing abnormalities. Also, past history of exposure to heavy metals, aromatic hydocarbons, and other chemicals was taken to supplement the trauma history. Present occupation was obtained when each tracing was made as a means of making sure that men in the control group did not handle borane fuels and to ensure that men in the study group were still handling borane fuels. A careful history of possible contact with boron hydrides was taken. This included duration of handling the fuels, time and frequency of exposure, and severity of the exposure. Because a separate history was taken after each tracing, a single exposure could have been described several times.

Comparison of the serial histories revealed discrepancies caused by memory loss through lapse of time. The history taken soon after an event was more likely to be concise than one taken nearly a year later. The most logical historical information available was used in reconstructing each man's exposure history at the termination of the study. Medical records, personal interviews, eyewitness accounts, and fuel laboratory log books were consulted to supplement and verify historical data. Lastly, a history of events occurring to the subject in the 24 hours preceding the tracing were recorded. Drug ingestion, flying, and the preceding meal were defined. The food history became unimportant once glucose was given routinely to ensure high blood sugar levels.

As a means of summarization of the exposure history, a calendar of maximum monthly exposure was compiled for each man. Chronology of exposure to boranes was recorded from January 1958 through February 1961. The following exposure classification was used for the monthly periods of work history:

0 Not working in areas where boranes were handled ("control")

1 Working in borane handling area

2 Exposed to borane vapor or spill without developing symptoms

3 Exposed to borane vapor or spill with symptoms resulting

No attempt was made to record exact date of exposure. The concentration in air to which the man was exposed always remained unknown. Since so little adequate medical followup of an exposed man was available, only the presence or absence of symptoms remembered by the subject was defined. This neglect of pertinent ancillary clinical information leaves much to be desired, but, unfortunately, little useful information was recorded at the time events occurred.

EEG-EXPOSURE CORRELATION

Electroencephalograms and exposure histories for 145 men were compiled for analysis. This figure included every person working at either North American Aviation, Inc., or Edwards Rocket Base for whom original serial EEG tracings could be obtained from any source. Of this group, only four pilots from North American Aviation, Inc., were not included in the final tabulation. Even though these men had not been in contact with borane fuels, they were not true "controls." It was decided that the abnormalities evident in their tracings, probably an effect of repeated in-flight trauma, would invalidate the control series if included. Only 22 men remained in the control group at Edwards Rocket Base at the end of the study. The remaining 119 men who had worked with boranes were approximately equally divided between the two participating organizations.

Most of the men in the study showed no change between serial EEG's. A few men's tracings showed changes which the electroencephalographer classed insignificant. The changes between theta, delta, and paroxysmal responses to hyperventilation fell in this category. The six persons exhibiting these minor changes were pooled with the group showing no change for further tabulation.

The prevalence of EEG changes in the controls and unexposed groups is quite similar (Table 1). However, the group who were exposed to vapor or spill appear to have a much greater prevalence of abnormal EEG's. Although the actual increase is quite small, it is thought to be clinically important. A further breakdown of this data is indicated even though the number of cases in each category is quite small.

TABLE 1

SUMMARY OF EEG CHANGES NOTED DURING SURVEY

	Persons Having Significant Change Between Tracings	Total Persons	Percent of Persons With Changes
Controls	4	22 23	18 17.4
Not Exposed but in area.	17	79	22 21.6
Exposed to Vapor or Spill	15	40 39	37 38.4

It should be noted (Table 2) that the percentage of persons having abnormal tracings which reverted to normal during the study was fairly uniform among control (18%), unexposed (18%), and exposed workers (22%). → 23%. One would be tempted to conclude that we are observing the same chance phenomenon in all three classifications. So what?

The conversion of a subject's tracing from normal to abnormal after exposure does not appear to be a chance occurrence, however. The control (0%) and unexposed (4%) groups had much less such changes than did the the exposed group (15%).

A presentation of numerical data does not give a complete clinical pattern of the exposure-EEG syndrome. It was thought appropriate to present case

TABLE 2

SUMMARY OF EEG FINDINGS ON PERSONS
PARTICIPATING IN THE STUDY

	No Change Noted	Abnormal Converted to Normal	Normal Converted To Abnormal	Clinically Insignificant Changes	Total
Control Group, ERB*	18	4	0	0	22
Fuel Handlers Not Exposed					
NAA**	28	4	2	3	37
ERB	28	10	1	3	42
Total	56	14	3	6	79
Fuel Handlers Exposed to Vapor or Spill					
NAA	16	5	5	0	26
ERB	9	4	1	0	14
Total	25	9	6	0	40
Total Entire Study Population	99	27	9	6	141

*ERB - Edwards Rocket Base, a facility of Edwards Air Force Base, Air Force Systems Command personnel.

**NAA - North American Aviation, Inc., Fuel Laboratory and Propulsion Field Laboratory personnel.

histories of the exposed 15 men showing EEG changes to allow the reader to draw his own conclusions. An effort has been made to incorporate all available information into the case histories. It is evident how meager this information actually was.

CASE HISTORIES

Patient 101

This 37-year-old research engineer gave a history of working with pentaborane since May 1958. Fourteen months later he was exposed to pentaborane vapors and developed symptoms leading to hospitalization. His initial symptoms were those of mental confusion and lack of coordination. He felt very sleepy. Repeated prothrombin times were consistently abnormal.

His initial EEG, taken 1 month after exposure, showed a generalized slow pattern on the resting tracing and a theta response to hyperventilation. He was questionably hypoglycemic at this time, so a repeat tracing was made 1 month later. The slow response remained the same, but the response to the hyperventilatory exercise was now normal. He was removed from the borane handling area immediately following exposure. A final tracing taken 19 months after exposure was entirely within normal limits.

Patient 102

This 40-year-old male fireman exhibited a normal EEG when entering the routine program of medical surveillance for pentaborane exposure. Four months after this initial tracing, he was exposed to a small spill of pentaborane. A followup tracing taken 6 months after exposure showed a normal resting pattern, but a theta response to hyperventilation was now evident.

Patient 108

This 40-year-old male fireman worked with pentaborane for 13 months before suffering his first exposure by inhalation. He did not develop symptoms from exposure. Two tracings, taken at intervals of 1 and 2 months after exposure, revealed an abnormal resting pattern suggesting a localized lesion. Theta response was produced by hyperventilation. The abnormalities had vanished by the time the final tracing was made 19 months after exposure.

Patient 119

This 30-year-old male test stand mechanic from Edwards Rocket Base had handled pentaborane for 9 months before his initial EEG was taken. The tracing was normal. Two months later he was exposed to pentaborane vapors but failed to develop symptoms. The following month his followup EEG still showed a normal resting pattern, but the response to hyperventilation now showed theta activity.

NOT So, see Record.

Patient 121

This 35-year-old male mechanic from Edwards Rocket Base worked on test stand 140 for only 2 months before he developed symptoms from inhaling pentaborane vapors. His initial EEG taken 2 months following exposure revealed evidence of a focal lesion on the resting tracing. Response to hyperventilation was normal. A repeat tracing 6 months after exposure showed the same focal lesion, but the response to hyperventilation now included theta activity. The last tracing, taken 13 months after the initial exposure, was entirely within normal limits.

Patient 123

This 42-year-old male engine-test mechanic worked with pentaborane for 18 months before being exposed by inhalation. He became symptomatic from this exposure, but no record of what symptoms developed is available. His initial EEG taken 1 year after exposure was abnormal. The generalized slow response on the resting tracing was accompanied by a theta response upon hyperventilation. Two tracings, taken 16 and 19 months after exposure were within normal limits.

Patient 127

This 40-year-old male test stand mechanic at Edwards Rocket Base was subjected to his first routine EEG in this study only 3 months after starting to work in the area. The tracing was abnormal. The resting record revealed a generalized slow pattern, while the hyperventilation portion showed theta activity. Three months later he was exposed to pentaborane vapors in sufficient concentration to develop symptoms. No record of his symptomatology is available. An EEG taken 1 month after exposure showed no change from the original trace. His routine EEG's taken 5 and 8 months after exposure were entirely within normal limits.

Patient 129

This 44-year-old engine test mechanic at Edwards Rocket Base was exposed to toxic concentrations of pentaborane vapors during his first month of working with the fuel. He developed symptoms from this exposure. His initial EEG taken 5 months later exhibited a normal resting pattern, but the response to hyperventilation contained theta activity. Followup tracings taken 13 and 16 months after exposure were within normal limits.

Patient 140

This 23-year-old male chemical engineer inhaled high-energy fuel but failed to develop symptoms. His initial EEG taken 3 months later was abnormal. Generalized slow waves were evident, but response to hyperventilation was normal. During the following 12 months he was repeatedly exposed to high-energy fuels, but never developed symptoms. His second EEG, which was taken at the termination of these exposures, again exhibited a generalized slow pattern, and, in addition, showed a theta response to hyperventilation. This pattern remained unchanged on a third tracing taken 9 months later.

Patient 141

This 38-year-old male research engineer worked for 7 months in the high-energy fuel laboratory before his first EEG was taken as part of the medical surveillance program. A normal resting tracing was obtained, but the delta response to hyperventilation was unexpected. A repeat surveillance tracing taken 11 months later had degenerated to abnormal. The generalized slow response show on the resting tracing was accompanied by a theta response to hyperventilation. He was exposed to high-energy fuel vapors 3 months later, but failed to develop symptoms. A final tracing taken 6 months after exposure showed a paroxysmal response on both the resting and exercise records.

Patient 142

This 23-year-old male research engineer inhaled high-energy fuel, becoming symptomatic. An EEG taken the following month was abnormal. Generalized slow waves characterized the tracing. A repeat tracing 12 months after exposure was normal. Both tracings revealed a delta response to hyperventilation.

Patient 143

This 25-year-old male research chemist states that he spent 20% of his working time in the East Parking Lot Fuel Laboratory. He had not been exposed to high-energy fuel vapors until one day, while observing a test firing, he was exposed to a low concentration. He failed to develop symptoms after this and a series of other small exposures scattered through the following 15 months.

At the time of each exposure, which lasted about 1 minute each, he detected a faint odor of high-energy fuel. His initial two EEG's were taken without assurance of an adequate blood sugar level. One revealed a normal resting pattern, while the other showed an abnormal generalized slow response. Both tracings exhibited a delta response to hyperventilation. A third tracing taken 1 month later with high blood sugar assured, again showed an abnormal slow resting pattern, but the response to hyperventilation was now normal. The resting tracing taken 10 months later was still abnormally slow; in addition, the response to hyperventilation showed theta activity.

Patient 144

This 43-year-old male industrial hygienist submitted to two routine EEG's as part of the medical surveillance program before initially exposed to high-energy fuel. Both tracings revealed a generalized slow response on the resting record and delta activity during hyperventilation. He developed symptoms after exposure to HEF vapor. Two months later his EEG tracing had changed slightly. The resting record remained the same, but theta activity was the only response to hyperventilation. He developed symptoms the following month after a repeat exposure. This warning was enough to remove him from the borane program. A final tracing taken 5 months after the last exposure was entirely within normal limits.

Patient 145

This 36-year-old male research chemist was exposed to high-energy fuel by inhalation in sufficient concentration to develop symptoms. Five months later his initial EEG was normal except for delta activity during hyperventilation. A short time later he was again exposed to high-energy fuel and became symptomatic. A followup EEG was abnormal. Generalized slow waves characterized the tracing.

Again hyperventilation precipitated delta activity. The following month he again developed symptoms after inhaling high-energy fuel. A repeat

EEG taken 9 months later showed no change. His EEG pattern had reverted to normal by the time another tracing was taken 18 months after his last exposure.

Patient 146

This 41-year-old male chemical engineer inhaled high-energy fuel vapors repeatedly over an 18-month period but failed to develop symptoms. Followup EEG's taken 1 and 12 months after the last exposure were abnormal. In addition to exhibiting a generalized slow pattern on the resting tracing, they showed delta activity during hyperventilation. Two tracings taken 14 months after exposure still exhibited the slow pattern, but response to hyperventilation was now normal.

SUMMARY AND CONCLUSIONS

A group of 119 rocket fuel handlers and 22 controls was followed through time by serial electroencephalograms. A total of 333 EEG records was tabulated. A complete data summary of the subjects is presented (Table 3).

Although observable, clinically important EEG changes were noted, the number of cases showing change was small. The pattern of central nervous system damage reconstructed from these few cases is as follows:

1. Known normals may convert to abnormal after exposure
2. Not all normals may convert to abnormal after the initial exposure, but may do so after repeated exposure
3. Post-exposure abnormalities tend to revert to normal about one year after exposure.

The EEG tracings showing post-exposure changes exhibit only slow activity in either or both the resting and hyperventilation record. Such abnormalities can be duplicated by many metabolic and infectious processes.

Experience from this project indicates a need for further controlled studies with animals where exposure dosage can be controlled and varied, and where adequate clinical observation is available.

TABLE 3

DATA SUMMARY

Subject Number	Age	EEG Interpretation[1]	Number of Records Interpreted	Maximum[2] Borane Exposure Classification
1	40	NHVO[3]	3	2
2	41	NHVO	3	2
3	47	NHVO	2	1
4	36	NHVO	3	✓3
5	43	NHVO	2	1
6	24	NHVO	3	2
7	28	NHVO	2	1
8	24	NHVO	2	2
9	44	NHVO	2	1
10	43	NHVO	2	1
11	39	NHVO	2	1
12	33	NHVO	2	1
13	27	NHVO	2	1
14	29	NHVO	2	1
15	31	NHVO	2	2
16	49	NHVO	2	1
17	29	NHVO	2	0
18	21	NHVO	2	0
19	24	NHVO	2	1
20	26	NHVO	2	0
21	22	NHVO	2	0
22	42	NHVO	2	1
23	48	NHVO	2	2
24	52	NHVO	2	1
25	37	NHVO	2	1
26	41	NHVO	2	1
27	35	NHVO	2	1
28	28	NHVO	2	1
29	29	NHVO	2	1
30	44	NHVO	2	0
31	28	NHVO	2	2

1, 2, and 3 see key at end of table

TABLE 3

(Continued)

Subject Number	Age	EEG Interpretation[1]	Number of Records Interpreted	Maximum[2] Borane Exposure Classification
32	45	NHVO[3]	3	2
33	26	NHVO	2	0
34	43	NHVO	2	1
35	51	NHVO	2	1
36	47	NHVO	3	2
37	34	NHVO	2	1
38	37	NHVO	2	1
39	45	NHVO	2	1
40	29	NHVO	2	0
41	18	NHVO	2	0
42	38	NHVO	2	1
43	44	NHVO	2	3
44	22	NHVO	2	0
45	35	NHVO	3	1
46	22	NHVO	2	0
47	32	NHVO	3	1
48	25	NHVO	2	0
49	41	NHVO	2	2
50	36	NHVO	3	1
51	28	NHVO	2	1
52	32	NHVO	2	0
53	29	NHVO	2	0
54	46	NHVO	2	1
55	26	NHVO	2	1
56	26	NHVO	2	0
57	42	NHVO	2	3
58	31	NHVO	2	3
59	45	NHVO	3	3
60	29	NHVO	2	0
61	21	NHVO	2	0
62	34	NHVO	2	1
63	24	NHVO	2	1
64	62	NHVO	2	1
65	40	NHVO	2	1
66	28	NHVO	2	1

1, 2, and 3 see key at end of table

TABLE 3

(Continued)

Subject Number	Age	EEG Interpretation[1]	Number of Records Interpreted	Maximum[2] Borane Exposure Classification
67	50	NHVO[3]	2	1
68	39	NHVO	2	1
69	26	NHVO	3	✓3
70	49	NHVO	2	✓3
71	43	NHVO	2	0
72	38	NHVO	2	1
73	52	NHVO	2	2
74	48	NHVO	2	1
75	54	NHVO	2	1
76	39	NHVO	2	1
77	25	NHVO	2	✓3
78	39	FHVO	2	✓3
79	25	SHVT	2	2
80	39	FHVO	2	1
81	34	LSHVD	3	✓ 3
82	34	SHVT	3	1
83	45	SHVT	2	✓3
84	31	SHVT	2	1
85	20	NHVT	2	1
86	38	SPHVT	2	1
87	36	FHVO	2	1
88	37	SHVT	3	1
89	24	SHVT	4	1
90	27	NHVT	2	0 ✓
91	25	NHVT	3	1
92	39	NHVT	3	1
93	22	NHVT	2	1
94	34	SHVT	2	1
95	20	SPHVT	2	0 ✓
96	31	SHVT	3	1
97	29	SHVD	2	2
98	28	SHVO	2	1
99	22	SLHVD	2	1
100	30	NHVO, NHVT	2	1

1, 2, and 3 see key at end of table

TABLE 3

(Continued)

Subject Number	Age	EEG Interpretation[1]	Number of Records Interpreted	Maximum[2] Borane Exposure Classification
		1 Mo. | 2 Mo | 19 Mo.		
* 101	38	(A) SHVT, SHVO, NHVO	3	✓3
* 102	40	NHVO, NHVT	2	2
103	44	SHVT, NHVO	2	1
104	24	NHVT, NHVO	2	1
105	37	NHVT, NHVO	2	1
106	34	SHVT, SHVD	2	1
107	29	SHVD, SHVT, SHVT	3	1
*108	40	B | LHVT, LHVT, NHVO	3	2
109	24	SHVT, NHVO	2	1
110	49	NHVO, SHVO, SHVO	3	1 –
112	30	NHVT, NHVO, NHVO	3	1
113	40	SHVT, NHVO, NHVO, NHVO	4	1
114	21	NHVT, NHVO	2	0 ✓
115	26	SHVD, SHVT, SHVD	3	1
116	23	NHVO, NHVT	2	1 –
117	20	NHVT, NHVO	2	0 ✓
118	23	NHVT, NHVO	2	1
*119	31	NHVO, SHVT	2	2
120	26	SHVD, SHVP, SHVT	3	1
* 121	36	LHVO, LHVT, NHVO	3	✓3
122	32	NHVT, NHVT, NHVO, NHVO	4	1
* 123	42	SHVT, NHVO, NHVO	3	✓3
124	24	NHVT, NHVO, NHVO	3	1
125	26	NHVT, NHVO	2	0 ✓
126	46	NHVD, NHVO, NHVO	3	1
* 127	40	SHVT, SHVT, NHVO, NHVO	4	✓3
128	40	NHVT, NHVO	2	0 ✓
*129	44	NHVT, NHVO, NHVO	3	✓3
130	23	NHVT, NHVO	2	1
131	45	SHVD, SHVT, NHVT	3	1
132	25	NHVT, NHVT, NHVO	3	1
133	25	NHVT, NHVO	2	1
134	30	SHVT, NHVO, NHVO, NHVT	4	1
135	22	PHVP, SHVT	2	1

1, and 2 see key at end of table

Note – Only 4/15 exposures had had baseline EEG's previous to definite exposure.

TABLE 3

(Continued)

136-139.

Subject Number	Age	EEG Interpretation[1]	Number of Records Interpreted	Maximum[2] Borane Exposure Classification
		3, 12, 21		
*140	23	SHVO, SHVT, SHVT 6	3	2
*141	38	NHVD, SHVT, PHVP 6	3	2
*142	23	SHVD, NHVD 12	2	√3
*143	25	NHVD, SHVD, SHVO, SHVT 1 10 2 5	4	2
*144	43	SHVD, SHVD, SHVT, NHVO	4	√3
*145	36	NHVD, SHVD, SHVD 9, NHVO 18 5	4	√3
*146	41	SHVD, SHVD, SHVO, SHVO	4	√3
		1, 12, 14, 14		

1. The interpretation is a combination of the resting and hyperventilation record. The first letter is the resting record; the last three letters refer to the hyperventilation record. NHVO means normal resting and normal hyperventilation.

EEG Resting Record

- N Normal
- S Slow
- F Fast
- L Focal or Locus
- P Paroxysmal

EEG Hyperventilation

- HVO Normal
- HVT Theta
- HVD Delta
- HVP Paroxysmal

2. 0 Not working in areas where boranes were handles
   1 Working in borane-handling areas
   2 Exposed to borane vapor or spill without developing symptoms
   3 Exposed to borane vapor or spill with symptoms resulting

3. Where more than one record was interpreted but only one interpretation is shown, all record interpretations were the same.

ASD TR 61-438

North American Aviation, Inc., Los Angeles, California
TOXICOLOGICAL RESEARCH ON CENTRAL NERVOUS SYSTEM EFFECTS OF BORANE FUEL, by C. E. Schoettlin, G. M. Cianko, R. D. Walter, and T. Freedman. July 1961. 42p. incl. illus., tables. (Proj. 7165; Task 71836) (Contract No. AF 33(616)-7186)
Unclassified report

This report describes the research conducted by North American Av iation, Inc., Los Angeles, California, on the central nervous system subsequent to accidental human exposure to boron hydrides. Serial electroencephalographic (EEG) tracings were used to identify the

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ASD TR 61-433

effects. Results of the study indicate little or no central nervous system damage was experienced by the participants. Methods, machines, and techniques used are described in detail. A complete data summary of all subjects tested is included.

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